WE CLAIM:

1. A synthetic RNA catalyst capable of cleaving an RNA substrate which contains the sequence:

$$5'\text{-}F_1\text{-}CS\text{-}F_2\text{-}3',$$

wherein,

CS is a cleavage sequence; and

$F_1$ and $F_2$ each is a sequence of bases flanking the cleavage sequence;

the catalyst comprising a substrate binding portion and a "hairpin" portion, the substrate binding portion of the catalyst having the sequence:

$$3'\text{-}F_4\text{-}L_1\text{-}F_3\text{-}5'$$

wherein,

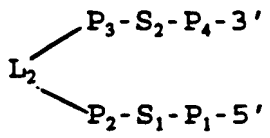
$F_3$ is a sequence of bases selected so that $F_3$ is substantially base paired with $F_2$ when the catalyst is bound to the substrate;

$F_4$ is a sequence of bases selected so that $F_4$ is substantially base paired with $F_1$ when the catalyst is bound to the substrate;

the sequences of $F_3$ and $F_4$ being selected so that each contains an adequate number of bases to achieve sufficient binding of the RNA substrate to the RNA catalyst so that cleavage of the substrate can take place; and

$L_1$ is a sequence of bases selected so that $L_1$ does not base pair with CS when the catalyst is bound to the substrate.

2. An RNA catalyst according to Claim 1, the "hair-pin" portion of the catalyst having the sequence:




wherein,

$P_1$ and $P_4$ each is a sequence of bases, the sequences of $P_1$ and $P_4$ being selected so that $P_1$ and $P_4$ are substantially base paired;

$P_1$ is covalently linked to $F_4$;

$S_1$ and $S_2$ each is a sequence of bases, the sequences of $S_1$ and $S_2$ being selected so that $S_1$ and $S_2$ are substantially unpaired;

$P_2$ and $P_3$ each is a sequence of bases, the sequences of $P_2$ and $P_3$ being selected so that $P_2$ and $P_3$ are substantially base paired; and

$L_2$ is a sequence of unpaired bases.

3. An RNA catalyst according to Claim 1 or 2 which is capable of cleaving an RNA substrate in which CS has the sequence 5'-NGUC-3', wherein N is any base and the substrate is cleaved by the catalyst between N and G.

4. An RNA catalyst according to Claim 3 wherein $L_1$ has the sequence 3'-AAGA-5'.

5. An RNA catalyst according to Claim 1 or 2 wherein $F_3$ is at least 3 bases in length and $F_4$ is from 3 to 5 bases in length, and the catalyst cleaves a substrate wherein $F_1$ and $F_2$ each is at least 3 bases in length.

6. An RNA catalyst according to Claim 5 wherein $F_3$ is from 6 to 12 bases in length and $F_4$ is 4 bases in

length, and the catalyst cleaves a substrate wherein $F_1$ is 4 bases in length and $F_2$ is from 6 to 12 bases in length.

7. An RNA catalyst according to Claim 2 wherein $P_1$ and $P_4$ each is from 3 to 6 bases in length.

8. An RNA catalyst according to Claim 7 wherein $P_1$ has the sequence 5'-ACCAG-3' and $P_4$ has the sequence 5'-CUGGUA-3'.

9. An RNA catalyst according to Claim 2 wherein $S_1$ and $S_2$ each is from 4 to 9 bases in length.

10. An RNA catalyst according to Claim 9 wherein $S_1$ has the sequence 5'-AGAAACA-3' and $S_2$ has the sequence 5'-GUAUAUUAC-3'.

11. An RNA catalyst according to Claim 2 wherein $P_2$ and $P_3$ each is from 3 to 9 bases in length.

12. An RNA catalyst according to Claim 11 wherein $P_2$ has the sequence 5'-CAC-3' and $P_3$ has the sequence 5'-GUG-3'.

13. An RNA catalyst according to Claim 2 wherein $L_2$ is at least 3 bases in length.

14. An RNA catalyst according to Claim 13 wherein $L_2$ has the sequence 5'-GUU-3'.

15. An RNA catalyst according to Claim 2 wherein 5'-$S_1$-$P_2$-$L_2$ has the sequence 5'AGAAACACACGUU-3'.

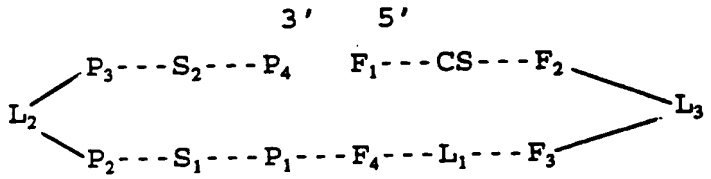
16. An RNA catalyst according to Claim 2 wherein 5'-$P_2$-$L_2$-$P_3$ has the sequence 5'-CACGGACUUCGGUCCGUG-3' [SEQ ID 46].

17. An RNA catalyst according to Claim 1 or 2 which is capable of cleaving an RNA substrate selected from the group consisting of messenger RNA, transfer RNA, ribosomal RNA, viral RNA, nuclear RNA, organellar RNA and other cellular RNA.

18. The catalyst of Claim 17 which is capable of cleaving an RNA substrate selected from the group consisting of HIV-1 virus RNA and tobacco mosaic virus RNA.

19. An RNA catalyst according to Claim 18 which is capable of cleaving HIV-1 RNAs containing the sequence UGCCCGUCUGUUGUGU.

20. An RNA catalyst according to Claim 2 containing the sequence:




wherein,

$F_1$, $F_2$, $F_3$, $F_4$, $L_1$, $L_2$, $S_1$, $S_2$, $P_1$, $P_2$, $P_3$ and $P_4$ are as defined in Claims 1 and 2; and

$L_3$ is a sequence of unpaired bases that covalently links the catalyst portion of the molecule with the substrate portion to produce a synthetic autocatalytic RNA catalyst.

21. An RNA catalyst according to Claim 20 wherein CS has the sequence 5'-NGUC-3', wherein N is any base, and the substrate is cleaved by the catalyst between N and G.

22. An RNA catalyst according to Claim 21 wherein $L_1$ has the sequence 3'-AAGA-5'.

23. An RNA catalyst according to Claim 22 wherein 5'-$P_1$-$S_1$-$P_2$-$L_2$-$P_3$-$S_2$-$P_4$-3' has the sequence 5'-ACCAGAGAAACACACGUUGUGGUAUAUUACCUGGUA-3'.

24. An RNA catalyst according to Claim 23 wherein $L_3$ has the sequence 3'-CCUCC-5'.

25. A synthetic RNA catalyst which is capable of cleaving an RNA substrate containing the sequence:

5'-$F_1$-CS-$F_2$-3',

the catalyst containing the sequence:

5'-$F_3$-$L_1$-$F_4$-ACCAGAGAAACACACGUUGUGGUAUAUUACCUGGUA-3',

and active variants thereof,

wherein,

CS is a cleavage sequence;

$F_1$ and $F_2$ each is a sequence of bases flanking the cleavage sequence;

$F_3$ is a sequence of bases selected so that $F_3$ is substantially base paired with $F_2$ when the catalyst is bound to the substrate;

$F_4$ is a sequence of bases selected so that $F_4$ is substantially base paired with $F_1$ when the catalyst is bound to the substrate;

the sequences of $F_3$ and $F_4$ being selected so that each contains an adequate number of bases to achieve sufficient binding of the RNA substrate to the RNA catalyst so that cleavage of the substrate can take place; and

$L_1$ is a sequence of bases selected so that $L_1$ does not base pair with CS when the catalyst is bound to the substrate.

26. A synthetic RNA catalyst which is capable of cleaving an RNA substrate containing the sequence:

$$5'\text{-}F_1\text{-CS-}F_2\text{-}3',$$

the catalyst containing the sequence:

$5'\text{-}F_3\text{-}L_1\text{-}F_4$-ACCAGAGAAACACACGGACUUCGGUCCGUG-
GUAUAUUACCUGGUA-3' [SEQ ID 47]

wherein,

CS is a cleavage sequence;

$F_1$ and $F_2$ each is a sequence of bases flanking the cleavage sequence;

$F_3$ is a sequence of bases selected so that $F_3$ is substantially base paired with $F_2$ when the catalyst is bound to the substrate;

$F_4$ is a sequence of bases selected so that $F_4$ is substantially base paired with $F_1$ when the catalyst is bound to the substrate;

the sequences of $F_3$ and $F_4$ being selected so that each contains an adequate number of bases to achieve sufficient binding of the RNA substrate to the RNA catalyst so that cleavage of the substrate can take place; and

$L_1$ is a sequence of bases selected so that $L_1$ does not base pair with CS when the catalyst is bound to the substrate.

27. An RNA catalyst according to Claim 25 or 26 wherein $F_3$ is at least 3 bases in length and $F_4$ is from 3 to 5 bases in length, and the catalyst cleaves a

substrate wherein $F_1$ and $F_2$ each is at least 3 bases in length.

28. An RNA catalyst according to Claim 27 wherein $F_3$ is from 6 to 12 bases in length and $F_4$ is 4 bases in length, and the catalyst cleaves a substrate wherein $F_1$ is 4 bases in length and $F_2$ is from 6 to 12 bases in length.

29. An RNA catalyst according to Claim 25 or 26 which is capable of cleaving an RNA substrate in which CS has the sequence 5'-NGUC-3', wherein N is any base and the substrate is cleaved by the catalyst between N and G.

30. AN RNA catalyst according to Claim 29 wherein $L_1$ has the sequence 3'-AAGA-5'.

31. An RNA catalyst according to Claim 25 or 26 which is capable of cleaving an RNA substrate selected from the group consisting of messenger RNA, transfer RNA, ribosomal RNA, viral RNA, nuclear RNA, organellar RNA and other cellular RNA.

32. An RNA catalyst according to Claim 31 which is capable of cleaving an RNA substrate selected from the group consisting of HIV-1 virus RNA and tobacco mosaic virus RNA.

33. An RNA catalyst according to Claim 32 which is capable of cleaving HIV-1 RNAs containing the sequence UGCCCGUCUGUUGUGU.

34. An engineered DNA molecule coding for an RNA catalyst according to Claim 1, 2, 20, 25 or 26.

35. A vector comprising a DNA sequence coding for an RNA catalyst according to Claim 1, 2, 20, 25 or 26,

the DNA sequence being operatively linked to expression control sequences.

36. The vector of Claim 35 which is capable of self-replication in a host.

37. The vector of Claim 35 wherein the RNA catalyst encoded by the vector is capable of cleaving an RNA substrate selected from the group consisting of messenger RNA, transfer RNA, ribosomal RNA, viral RNA, nuclear RNA, organellar RNA and other cellular RNA.

38. The vector of Claim 37 wherein the RNA catalyst encoded by the vector is capable of cleaving an RNA substrate selected from the group consisting of HIV-1 virus RNA and tobacco mosaic virus RNA.

39. The vector of Claim 38 wherein the RNA catalyst encoded by the vector is capable of cleaving HIV-1 RNAs containing the sequence UGCCCGUCUGUUGUGU.

40. A host cell transformed with a vector according to Claim 35 and which is capable of expressing the RNA catalyst.

41. A method of cleaving an RNA substrate which contains the sequence:

$$5'F_1\text{-}CS\text{-}F_2\text{-}3',$$

wherein,

CS is a cleavage sequence; and

$F_1$ and $F_2$ each is a sequence of bases flanking the cleavage sequence;

the method comprising contacting the substrate with a synthetic RNA catalyst comprising a substrate binding portion and a "hairpin" portion, the substrate binding portion of the catalyst having the sequence:

$$3'F_4\text{-}L_1\text{-}F_3\text{-}5'$$

wherein,

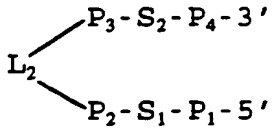
$F_3$ is a sequence of bases selected so that $F_3$ is substantially base paired with $F_2$ when the catalyst is bound to the substrate;

$F_4$ is a sequence of bases selected so that $F_4$ is substantially base paired with $F_1$ when the catalyst is bound to the substrate;

the sequences of $F_3$ and $F_4$ being selected so that each contains an adequate number of bases to achieve sufficient binding of the RNA substrate to the RNA catalyst so that cleavage of the substrate can take place; and

$L_1$ is a sequence of bases selected so that $L_1$ does not base pair with CS when the catalyst is bound to the substrate.

42. The method of Claim 41 wherein the "hairpin" portion of the catalyst has the sequence:




wherein,

$P_1$ and $P_4$ each is a sequence of bases, the sequences of $P_1$ and $P_4$ being selected so that $P_1$ and $P_4$ are substantially base paired;

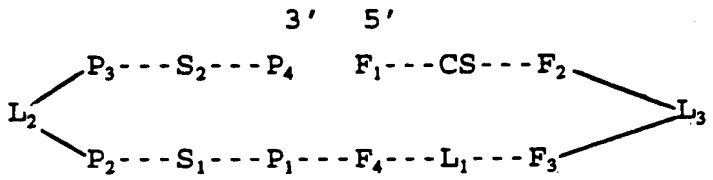
$P_1$ is covalently linked to $F_4$;

$S_1$ and $S_2$ each is a sequence of bases, the sequences of $S_1$ and $S_2$ being selected so that $S_1$ and $S_2$ are substantially unpaired;

$P_2$ and $P_3$ each is a sequence of bases, the sequences of $P_2$ and $P_3$ being selected so that $P_2$ and $P_3$ are substantially base paired; and

$L_2$ is a sequence of unpaired bases.

43. The method of Claim 42 wherein the catalyst has the sequence:




wherein,

$F_1$, $F_2$, $F_3$, $F_4$, $L_1$, $L_2$, $S_1$, $S_2$, $P_1$, $P_2$, $P_3$ and $P_4$ are as defined in Claims 41 and 42; and

$L_3$ is a sequence of unpaired bases that covalently links the catalyst portion of the molecule with the substrate portion to produce a synthetic autocatalytic RNA catalyst.

44. A method of cleaving an RNA substrate containing the sequence:

5'-$F_1$-CS-$F_2$-3',

comprising contacting the substrate with a synthetic RNA catalyst containing the sequence:

5'-$F_3$-$L_1$-$F_4$-ACCAGAGAAACACACGUUGUGGUAUAUUACCUGGUA-3',

and active variants thereof, wherein,

CS is a cleavage sequence;

$F_1$ and $F_2$ each is a sequence of bases flanking the cleavage sequence;

$F_3$ is a sequence of bases selected so that $F_3$ is substantially base paired with $F_2$ when the catalyst is bound to the substrate;

$F_4$ is a sequence of bases selected so that $F_4$ is substantially base paired with $F_1$ when the catalyst is bound to the substrate;

the sequences of $F_3$ and $F_4$ being selected so that each contains an adequate number of bases to achieve sufficient binding of the RNA substrate to the RNA catalyst so that cleavage of the substrate can take place; and

$L_1$ is a sequence of bases selected so that $L_1$ does not base pair with CS when the catalyst is bound to the substrate.

45. A method of cleaving an RNA substrate containing the sequence:

$$5'\text{-}F_1\text{-CS-}F_2\text{-}3',$$

comprising contacting the substrate with a synthetic RNA catalyst containing the sequence:

5'-$F_3$-$L_1$-$F_4$-ACCAGAGAAACACACGGACUUCGGUCCGUGG-
UAUAUUACCUGGUA-3' [SEQ ID 47]

wherein,

CS is a cleavage sequence;

$F_1$ and $F_2$ each is a sequence of bases flanking the cleavage sequence;

$F_3$ is a sequence of bases selected so that $F_3$ is substantially base paired with $F_2$ when the catalyst is bound to the substrate;

$F_4$ is a sequence of bases selected so that $F_4$ is substantially base paired with $F_1$ when the catalyst is bound to the substrate;

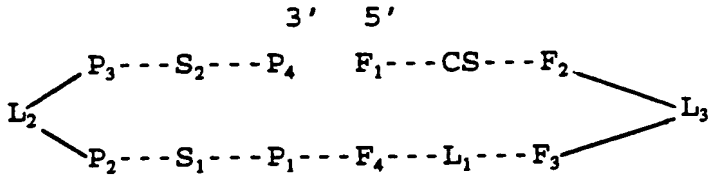
the sequences of $F_3$ and $F_4$ being selected so that each contains an adequate number of bases to achieve sufficient binding of the RNA substrate to the RNA catalyst so that cleavage of the substrate can take place; and

$L_1$ is a sequence of bases selected so that $L_1$ does not base pair with CS when the catalyst is bound to the substrate.

46. The method of Claim 41, 42, 43, 44 or 45 wherein the cleavage occurs under physiological conditions.

47. The method of Claim 46 wherein the cleavage occurs <u>in vivo</u> in a host cell which has been transformed with a vector comprising a DNA sequence coding for the RNA catalyst, the DNA sequence being operatively linked to expression control sequences.

48. A synthetic RNA transcript comprising an autocatalytic portion which has the formula:




wherein,

CS is a cleavage sequence;

$F_1$ and $F_2$ each is a sequence of bases flanking the cleavage sequence;

$F_3$ is a sequence of bases selected so that $F_3$ is substantially base paired with $F_2$;

$F_4$ is a sequence of bases selected so that $F_4$ is substantially base paired with $F_1$;

the sequences of $F_3$ and $F_4$ being selected so that each contains an adequate number of bases to achieve sufficient binding with $F_1$ and $F_2$ so that cleavage can take place;

$L_1$ is a sequence of bases selected so that $L_1$ does not base pair with CS;

$P_1$ and $P_4$ each is a sequence of bases, the sequences of $P_1$ and $P_4$ being selected so that $P_1$ and $P_4$ are substantially base paired;

$S_1$ and $S_2$ each is a sequence of bases, the sequences of $S_1$ and $S_2$ being selected so that $S_1$ and $S_2$ are substantially unpaired;

$P_2$ and $P_3$ each is a sequence of bases, the sequences of $P_2$ and $P_3$ being selected so that $P_2$ and $P_3$ are substantially base paired;

$L_2$ is a sequence of unpaired bases; and

$L_3$ is a sequence of unpaired bases.

49. A method of terminating an RNA transcript comprising:

transforming a host cell with a vector comprising DNA coding for an RNA transcript according to Claim 48;

culturing the host cell so that RNA is transcribed and the autocatalytic portion cleaves the RNA transcript to terminate the transcript.